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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,341	10/20/2005	Jian Liu	421/67 PCT/US	2710
7590 07/12/2007 Arles A Taylor Jr Jenkins Wilson & Taylor Suite 1400 University Tower 3100 Tower Boulevard Durham, NC 27707			EXAMINER SHEN, WU CHENG WINSTON	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/520,341	<b>Applicant(s)</b> LIU ET AL.	
	<b>Examiner</b> Wu-Cheng Winston Shen	<b>Art Unit</b> 1632	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 April 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-60 is/are pending in the application.
- 4a) Of the above claim(s) 5-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f):
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This application 10/520,341 is a 371 of PCT/US03/21094 07/07/2003, which claims benefit of 60/394,199, filed on 07/05/2002. Claims 1-60 are pending.

#### ***Election/Restriction***

1. Applicant's election of Group I, claims 1-4, drawn to an isolated and purified biologically active heparan sulfate 3-*O*-sulfotransferase 5 polypeptide, wherein the polypeptide comprises: (a) a polypeptide encoded by a nucleic acid sequence as set forth in SEQ ID NO 1; (b) a polypeptide encoded by a nucleic acid sequence having greater than 90% sequence identity to SEQ ID NO 1; (c) a polypeptide having an amino acid sequence as set forth in SEQ ID NO 2; (d) a polypeptide which is a biological equivalent of the polypeptide set forth in SEQ ID NO 2; (e) a polypeptide which is immunologically cross-reactive with an antibody which is immunoreactive with a polypeptide comprising part or all of the amino acids of SEQ ID NO 2; **or** (f) a polypeptide encoded by a nucleic acid molecule capable of hybridizing under stringent conditions to a nucleic acid molecule comprising the nucleotides of SEQ ID NO 1, or a complement thereof, in the reply filed on 04/10/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 5-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

***Status of claims:*** Claims 1-4 are currently under examination.

***Claim Objections***

2. Claim 4 is objected to because of the following informalities: Claim 4 is awkward as written. While it is clear what Applicant is intending to claim, the use of the term modified is not specifically recited to relate back to the polypeptide. The claim should recite "wherein the polypeptide is modified to be in detectably labeled form". Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 2, 3, and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is unclear in term of the metes and bounds of the related limitations between (a), (b), (c), (d), and (e). The word "or" is stated in limitations (e) and (f). Accordingly, the Examiner's interpretation of claim 2 as stated is as follows: An isolated and purified biologically active heparan sulfate 3-O-sulfotransferase 5 polypeptide, wherein the polypeptide comprises: (a) or (b) or (c) or (d) or (e). However, claim 2 as stated can read on other interpretations, including, for instance, [(a) and (b) and (c)] and [(e) or (f)]. Clarification with respect to the metes and bounds of claim 2 is required.

Claim 3 is unclear as to whether it is drawn to heparan sulfate 3-O-sulfotransferase 5 polypeptide isolated from any species of animal wherein said heparan sulfate 3-O-

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sulfotransferase 5 polypeptide further comprises human heparan sulfate 3-*O*-sulfotransferase 5 polypeptide or whether the claim is intended to read “wherein the polypeptide is human heparan sulfate 3-*O*-sulfotransferase 5 polypeptide”

Claim 4 is unclear because the specification does not define what “detectably labeled form” is.

***Claim Rejection - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***Written description***

4. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims 1-4, in light of disclosure in the specification discussed in the preceding section of rejection under the first paragraph of 35 U.S.C. 112, encompass an isolated and purified biologically active heparan sulfate 3-*O*-sulfotransferase 5 polypeptide. Claim 2 is drawn to fragments, mutated, and allelic variants of an isolated and purified biologically active heparan sulfate 3-*O*-sulfotransferase 5 polypeptide, while claims 3 and 4 are drawn to human heparan sulfate 3-*O*-sulfotransferase polypeptide, and labeled from of heparan sulfate 3-*O*-

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sulfotransferase polypeptide respectively. *At the time of filing, only heparan sulfate 3-O-sulfotransferase 5 polypeptide isolated from human was disclosed. The claims do not set forth any structural requirements for biologically active heparan sulfate 3-O-sulfotransferase 5 polypeptide, including the amino acid residues required for the enzymatic activity.* When the claims are analyzed in light of the specification, the invention encompasses a genus of polypeptide molecules encoded by enormous number nucleotide molecules, which are *as yet undisclosed or undiscovered*. The specification teaches the 3-OST-5 polypeptide isolated from human placenta cDNA library, but fails to teach any fragments, variants or nucleic acids that hybridize to a nucleic acid encoding 3-OST-5 that would have the same functional characteristics as the 3-OST-5 polypeptide disclosed in the specification (SEQ ID NO:2).

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been disclosed. The instant specification teaches human 3-OST-5 (SEQ ID NO 2), and no other species encompassed by the genus of 3-OST-5 fragments or variants encompassed by the claims.

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. other nucleotide sequences or positions within a specific gene or nucleic acid), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case the specification only provides putative structural limitation required for being a 3-OST via indication of conserved amino acid residues by the alignment of human 3-OST-5 (SEQ ID NO 2), and 3-OST-1, 3-OST-3A, and 3-OST-3B (SEQ ID NOs 3, 4 and 5). However, there is no information disclosed in the specification regarding polypeptide comprising the amino acid residues required

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for the enzymatic activity and the nucleic acid encoding the required amino acid residues. There is no evidence on the record of a relationship between the structures of the nucleotide sequences coding for the 3-OST-5 variants or fragments encompassed by claim 2 and the nucleotide sequence set forth by SEQ ID NO: 2 that would provide any reliable information about the structure of polypeptide molecules within the genus. The claimed invention as a whole is not adequately described if the claims require essential or critical elements that are not adequately described in the specification and that is not conventional in the art as of applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641,1646 (1998). The claims read in light of the specification encompass any nucleic acid molecule encoding any polypeptides with detectable 3-OST-5 enzymatic activity as assayed by incubating different fractions separated from Heparin-Sepharose chromatography with medium from cells as starting material for purification of 3-OST-5 with unlabeled heparin sulfate (HS) and [<sup>35</sup>S] PAPS to generate [<sup>35</sup>S] HS *in vitro* (see paragraph[ 0036]). However, this disclosed assay in specification fails to demonstrate the assay is specific for 3-OST-5, and fail to demonstrate that the assay is not indicative of the presence of other isoforms of 3-OST as well. In this regard, applicant is encouraged to clarify, for instance, the distinction between the assay disclosed in the specification for 3-OST-5 and the assay described by Munoz et al. (Munoz et al. Affinity, kinetic, and structural study of the interaction of 3-O-sulfotransferase isoform 1 with heparan sulfate. *Biochemistry*, 45(16):5122-8, 2006).

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In the instant application, the provided information regarding nucleic acid SEQ ID No: 1 (1041 nucleotides which encodes SEQ ID No: 2), SEQ ID No: 2 (346 amino acid residues), and SEQ ID NOs 3, 4 and 5 (corresponding to 3-OST-1, 3-OST-3A, and 3-OST-3B), do not constitute an adequate written description of the broad subject matter of the claims, and so one of skill in the art cannot envision the detailed chemical structure of the polypeptides encoded by nucleic acids encompassed by the claimed heparan sulfate 3-*O*-sulfotransferase polypeptide. Adequate written description requires more than a statement that nucleic acids and polypeptides with a particular quality are part of the invention and reference to a potential method for their identification. The nucleic acid and polypeptide sequences are required.

In conclusion, the limited information provided regarding heparan sulfate 3-*O*-sulfotransferase polypeptide encoded by nucleic acid is not deemed sufficient to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)



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The skilled artisan cannot envision the detailed chemical structure of the encompassed [nucleic acids, polymorphisms, amino acids, etc, use what is appropriate for the situation] regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993), and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. The current situation is a definition of the compound solely based on its functional utility, as a polymorphism, without any definition of the particular polymorphisms claimed.

Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that, "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606

(Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

### *Scope of Enablement*

5. Claims 1, 2 and 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated and purified biologically active heparan sulfate 3-*O*-sulfotransferase 5 polypeptide wherein the polypeptide catalyzes the reactions generating at least three 3-*O*-sulfated disaccharides as follows: IdoUA2-AnMan3S, GlcUA-AnMan3S6S, and IdoUA2S-AnMan3S6S, **does not** reasonably provide enablement for (1) any fragments of polypeptide encoded by a nucleic acid sequence as set forth in SEQ ID NO 1; (2) any fragment of a polypeptide encoded by a nucleic acid sequence having greater than 90% sequence identity of SEQ ID No 1; (3) any fragments of polypeptide having an amino acid sequence as set forth in SEQ ID NO 2; (4) any fragments of polypeptide which is a biological equivalent of the polypeptide set forth in SEQ ID NO 2; (5) any fragment of a polypeptide which is immunologically cross-reactive with an antibody which is immunoreactive with a polypeptide comprising part or all of the amino acids of SEQ ID NO 2; or (6) any polypeptide encoded by a nucleic acid molecule capable of hybridizing under stringent conditions to a nucleic acid molecule comprising the nucleotides of SEQ ID NO 1, or a complement thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue

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experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The nature of the instant invention is an isolated and purified biologically active heparan sulfate 3-*O*-sulfotransferase isoform 5 polypeptide. The breadth of the claims, in light of specification, encompasses isolated and purified biologically active heparan sulfate 3-*O*-sulfotransferase 5 polypeptides.

The specification disclosed the terms "3-OST-5 gene product", "3-OST-5 protein", and "3-OST-5 polypeptide" also include analogs of HS D-glucosaminyl-3-*O*-sulfotransferase isoform 5 molecules. By "analog" is intended that a DNA or peptide sequence can contain alterations relative to the sequences disclosed herein, yet retain all or some of the biological activity of those sequences. Analogs can be derived from genomic nucleotide sequences as are

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disclosed herein or from other organisms, or can be created synthetically. Those skilled in the art will appreciate that other analogs, as yet undisclosed or undiscovered, can be used to design and/or construct 3-OST-5 analogs. There is no need for a "3-OST-5 gene product", "3-OST-5 protein", and "3-OST-5 polypeptide" to comprise all or substantially all of the amino acid sequence of a native 3-OST-5 gene product. Shorter or longer sequences are anticipated to be of use in the invention; shorter sequences are herein referred to as "segments." Thus, the terms "3-OST-5 gene product", "3-OST-5 protein", and "3-OST-5 polypeptide" also include fusion or recombinant HS D-glucosaminyl-3-O-sulfotransferase isoform 5 polypeptides and proteins comprising sequences of the present invention (See (paragraphs [0067])). The specification also disclosed a multiple amino acid sequence alignment of human 3-OST-5 (SEQ ID NO 2) with human 3-OST-1, 3-OST-3A, and 3-OST-3B (SEQ ID NOs 3, 4 and 5, respectively) in Figure 2 (See paragraph [0029]), and that the activity of 3-OST-5 was monitored by incubating the eluent (10  $\mu$ l) with unlabeled heparin sulfate (HS) and [ $^{35}$ S] PAPS to generate [ $^{35}$ S] HS. It is noted that PAPS is a coenzyme of 3-OST enzymes, which stands for 3'-phosphoadenosine 5'-phosphosulfate (See paragraph [0036]).

With regard to lack of enablement support for (1) any fragments of polypeptide encoded by a nucleic acid sequence as set forth in SEQ ID NO 1, (2) any fragment of a polypeptide encoded by a nucleic acid sequence having greater than 90% sequence identity of SEQ ID No 1, (3) any fragments of polypeptide having an amino acid sequence as set forth in SEQ ID NO 2, (4) any fragments of polypeptide which is a biological equivalent of the polypeptide set forth in SEQ ID NO 2, and (5) any fragment of a polypeptide which is immunologically cross-reactive with an antibody which is immunoreactive with a polypeptide comprising part or all of the

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amino acids of SEQ ID NO 2, it is noted that the specification does not provide any working example other than full length of SEQ ID No 2 (346 amino acid residues) being biologically active as an 3-OST enzyme (Examples 7- 9 of instant application). Accordingly, for an artisan to use or make the instantly claimed functional fragments or functional equivalent variants, an artisan would first have to identify if the sequences had 3-OST enzymatic activity. The claim encompasses nucleic acid encoding fragments of SEQ ID NO: 2 as well as nucleic acids with greater than 90% sequence identity to that encoding a fragment of SEQ ID NO:2, including fragments as small as 10 nucleotides or smaller. The level of experimentation to determine which of the fragments would encode 3OST-5 enzymatic activities would be undue.

Also since the functional domain necessary and sufficient for the 3-OST-5 enzymatic activity is not disclosed, an artisan would not know which sequences would need to be conserved in a biological equivalent of SEQ ID NO: 2 to render the equivalent biological function as claimed. An artisan would not know which 10% of the sequence could be different from polypeptide sequence of SEQ ID NO: 2 and still retain the function of the claimed 3-OST-5 enzymatic activity. Therefore, an artisan would not know how to make a biological equivalent wherein the nucleic acid having greater than 90% sequence identity to nucleotides 1-1041 of SEQ ID NO: 1.

Therefore, given that the specification and art lack specific guidance to the necessary and sufficient functional domain of the 3-OST-5 enzyme disclosed, an artisan would have to do further in vitro studies to determine which part of the sequence are the necessary and sufficient functional domain of the 3-OST-5 enzyme and this level of empirical experimentation would be considered undue.

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The instant invention is also drawn to any polypeptide encoded by a nucleic acid molecule capable of hybridizing under stringent conditions to a nucleic acid molecule comprising the nucleotides of SEQ ID NO 1, or a complement thereof. However, the state of the art suggests that sequences identified by their hybridization properties are unpredictable in their identity in sequence to the original sequence to which it hybridized. **Kennell** (Principles and practices of nucleic acid hybridization. *Prog Nucleic Acid Res Mol Biol.* 11:259-301, 1971) teaches that 25 to 50% nucleic acid identity is all that is necessary for hybridization of a sequence under any conditions and that obtaining non-specific hybridization products are highly common in the art (par bridging p. 260 and 261 and par 1 of p. 261). The specification provides general guidelines and conditions for obtaining hybridization products. However, these condition are exemplary and not limiting. Furthermore, these general guidelines and conditions provided by the specification do not provide any guidance to overcome the unpredictabilities described in the art. Therefore, an artisan would not know if a sequence that hybridized to the nucleotides of 1-1041 of SEQ ID NO: 1 would be a true complementary sequence capable of encoding a 3-OST enzyme or a non-specific hybridization product. Furthermore, for an artisan to use or make the claimed nucleic acid capable of hybridizing to the nucleotides of 1-1401 of SEQ ID NO: 1, they would first have to sequence the product to determine if it was a true complement and then also test the functionality of the nucleotide for its 3-OST enzymatic activity. This level of experimentation would be considered undue. Furthermore, even if a nucleic acid sequence meet the limitations of having greater than 90% sequence identity to the full length of SEQ ID 1 and hybridizes to SEQ ID 1 under exemplary stringent hybridization conditions as disclosed in instant application (See paragraphs [0077]), the nucleic acid sequence

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may not have 3-OST enzymatic activity. In this regard, for instance, **Munoz et al.** teach that single point mutations R72A, R67A, and K123A result in 3-OST-1 mutants that are inactive (See Figure 3B, and Discussion, bridging paragraph of columns, Munoz et al. Affinity, kinetic, and structural study of the interaction of 3-O-sulfotransferase isoform 1 with heparan sulfate, *Biochemistry*, 45(16): 5122-8, 2006).

In view of the state of the art, the unpredictability in the art, and the lack of specific guidance and working examples in the specification, one of skill in the art would have to perform undue experimentation to make and use the invention commensurate in scope with these claims 1-4 of instant application.

### ***Conclusion***

6. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent

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Examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

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AU 1632